REMARKS

Claims 17-26 are currently pending.

Claims 1-10 and 13, previously pending, are cancelled without prejudice to the prosecution of their subject matter in other applications.

New claims 17-26 are added to focus and advance the prosecution of this application. The new claims are supported by the specification and claims as originally filed, including, but not limited to, page 5 lines 6-15, page 5 lines 16-21, page 5 lines 24-25, page 10 lines 15-23, and original claims 9 and 10. None of the new claims constitute new matter.

The claims are rejected as indefinite, anticipated, and/or obvious. For reasons discussed below, it is requested that all the rejections be removed and that the claims be allowed to issue.

1. The Certified Priority Document Was Submitted

The Examiner has indicated that a certified copy of priority Austrian application A 89/2001, as required, is missing in the instant image file wrapper of the above-identified application.

Applicants note that a certified copy of the Austrian priority document was in fact submitted on December 9, 2003. In addition, a copy of this submission, including the certified copy of the priority document, was available in the Image File Wrapper; a copy has been printed out and is submitted herewith as Exhibit A.

Accordingly, it is believed that the priority claim has been perfected and that no additional submissions are required.

2. The New Claims Are Not Indefinite

Claims 2-10 and 13 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the alleged failure to further limit the claimed drug composition. The Examiner contends that it is unclear whether certain recited materials are comprised in, or in addition to, the microparticles.

Applicants assert that the basis for this rejection is obviated by the new claims. It is requested that the rejection be removed.

3. The Claims Are Not Anticipated By Knighton

Claims 1-9 are rejected under 35 U.S.C. 102(b) as anticipated by United States Patent No. 5,165,938 by Knighton ("Knighton").

According to the Examiner, Knighton dislcloses a composition, prepared from blood, which is intended for topical application to promote wound healing. The Examiner contends that Knighton teaches a drug composition that contains "microparticles," derived from platelet-rich plasma after activation and centrifugation, mixed with microcrystalline collagens and frozen, which is made under sterile conditions and can further contain growth factors. Substances such as fibrinogen, thrombin, glycoproteins, and inorganic compounds are, according to the Examiner, inherently present.

To be anticipatory, a single reference much teach each and every element of the claims. In the case at hand, Knighton, while teaching thrombocyte activation, does not separate microparticles *from* the supernatant into which they are released. Rather, Knighton mixes the supernatant of activated thrombocytes with a carrier such as microcrystalline collagen to form a paste. In contrast, the new claims specify that microparticles are "prepared by a process

comprising . . . collecting the microparticles *from* the liquid medium by a method selected from the group consisting of differential centrifugation, filtration and affinity chromatography." Because Knighton does not teach this separation step, it cannot anticipate the claims.

Accordingly, the rejection should be removed.

4. The Claims Are Not Anticipated By Chao

Claims 1-4 and 6-9 are rejected under 35 U.S.C. §102(b) as anticipated by United States Patent No. 5,185,160 by Chao ("Chao"). According to the Examiner, Chao discloses a pharmaceutical composition comprising viral-inactivated blood platelet membrane microparticles separated by sequential centrifugations which are subjected to virus inactivation by heat and where the composition is prepared under sterile conditions and provided in a frozen or lyophilized state. The Examiner contends that inorganic compounds, fibrinogen and thrombin are inherently present. The Examiner states:

> Although the particular application of the cited product relates to transfusion as intended to reduce bleeding time, the bleeding reducing drug would clearly be suitable in wound healing. The differences between drug composition as intended for transfusion and as intended for topical application would relate to carriers (inactive ingredient) or to dosage of active ingredient. The claimed invention is not so limited.

The Examiner has not been persuaded by Applicants' previous argument that the "microparticles" disclosed in Chao are not the same as those taught by the instant application, because the starting platelets utilized in Chao were not activated. The Examiner states This argument is not found particularly convincing because the [Chao's'] "microparticles" are platelet membrane microvesicles (see title) that are obtained by freeze thawing of platelets. It is known that the blood platelets are activated by freeze thawing as evidenced by Exner et al.

Applicants disagree with the Examiner's position, and maintain that the microparticles of the present invention are not the same as those of Chao. As stated in their previous response, platelets, once activated, release microparticles, which are heterogenic in size. Wolf, Br J Haematol 1967;13:269-288 (attached as Exhibit 1 in the Response filed December 4, 2006). For example, in platelets, microparticle release may be stimulated by epinephrine, adenosine diphosphate, thrombin, collagen, Ca2+ ionophore A23187, complement complex C5b-9, and/or antiplatelet antibodies. Applicants assert that microparticle shedding according to the invention is a controlled process induced by cell activation, and the microparticles so produced differ from those produced by Chao's freeze-thawing procedure.

Applicants' disagreement notwithstanding, the new claims now require that activation be achieved via "thrombin, collagen, calcium ionophore A23187 and C5b-9" - *not freeze-thawing.* By failing to teach the use of these activating agents, Chao cannot anticipate the claims.

In addition, it is noted that Chao, like Knighton, retains the microparticles in a supernatant and does not collect the microparticles *from* the liquid medium as required by the instant claims.

Accordingly, the rejection should be withdrawn.

5. The Claims Are Not Obvious

Claims 1-10 and 13 are rejected under 35 U.S.C. §103(a) as obvious over Knighton and Chao taken with United States Patent No. 5,697,980 by Otani et al. ("Otani"). The Examiner contends that although Knighton and Chao are missing disclosure of titanium, apatite and organic polymers, these elements are provided by Otani, characterized as teaching artificial

filing and prosthetic devices capable of adhering to tissues and materials such as titanium core coated with calcium phosphate and organic polymers such as polycaprolactone or polyactone. According to the Examiner, it would have been obvious to add various carriers, fillings, biodegradable materials and devices to modify the compositions of Knighton and Chao with a reasonable expectation of success in wound healing.

Applicants disagree for a number of reasons.

Applicants assert that the claims are not obvious, and respectfully submit that, as set forth in Graham v. J. Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), there are several steps that must be followed in order to properly establish an obviousness rejection under 35 U.S.C. § 103. First the scope and content of the prior art are to be determined, then any differences between the prior art and the claims at issue are to be ascertained, and finally the level of ordinary skill in the pertinent art is resolved. It is against this background that the obviousness or nonobviousness of the subject matter is determined by identifying whether one of ordinary skill in the art would have a reasonable expectation of success in achieving the claimed invention by making the proposed combination. (M.P.E.P. §2143; In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)). Although the Supreme Court has recently asserted that these "Graham Factors" are to be analyzed in a flexible manner, taking into consideration the common knowledge and common sense of those of ordinary skill in the art, Applicants note that the Court specifically stated that the above-described factors are consistent with an appropriate test for establishing obviousness. (KSR v. Teleflex, US 550 U.S. __, slip opinion at 15-17 (2007)).

The Examiner has understated the differences between the cited art and the claimed invention. Chao, for example, relates to procoagulant preparations to be administered by transfusion to treat thrombocytopenia. Even though it might be argued that an agent that

would be applied to a wound to promote healing might have procoagulant activity, this is not always the case (often wound-healing agents are applied after bleeding is stopped). Moreover, there may be a substantial difference in the degree of procoagulant activity. If a procoagulant substance is to be applied to a wound, presumably it would be desirable that it rapidly stop bleeding. Such an agent, transfused into the blood stream, could provoke a clinical disaster by eliciting uncontrolled thrombosis. The Examiner has seemingly not considered such issues.

As regards Knighton, the Examiner has not considered that Knighton produces its wound healing composition by creating a paste from a microparticle containing supernatant and microcrystalline collagens. Thus, Knighton essentially creates a bandage. This is different from the present invention, the crux of which involves using microparticles to promote the proliferation of wound-healing cells, together with provisional extracellular matrix materials to provide a carrier substance for growth factors as well as a scaffold for immigrating cells (see the specification at page 4, lines 28-29 and page 5 lines 18-21).

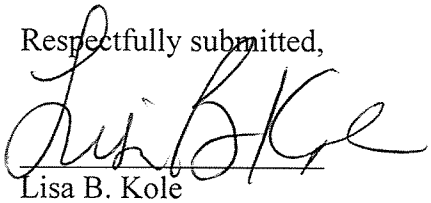
The skilled artisan would not consider combining the product of Chao, which is intended for transfusion, with the artificial filling/prosthetic material of Otani (rather, the combination of a transfusible substance with such materials would be contrary to its intended use). As regards the paste of Knighton, its application to a substrate would seem to merely reinforce the structural aspects of Knighton's products.

Accordingly, the skilled artisan would have no reason to expect that the claimed composition, in view of Knighton, Chao, Otani or any combination thereof, would be successful in promoting wound healing. Therefore, the rejection should be removed.

6. CONCLUSION

For all the foregoing reasons, the rejections should be removed and the claims should be allowed to issue.

Respectfully submitted,



Lisa B. Kole
Patent Office Reg. No. 35,225

Van H. Nguyen
Patent Office Reg. No. 56,571

Attorneys for Applicants
BAKER BOTTS L.L.P.
30 Rockefeller Plaza
New York, NY 10112--4498
(212) 408-2500